

18. (Once Amended) A method of specifically cleaving an RNA in a cell containing RNase H which comprises administering an effective amount of an oligonucleotide complementary to the RNA comprising: a 5' terminus; a 3' terminus; and from 11 to 59 5' → 3'-linked nucleotides which contiguously hybridize to the RNA and which are independently selected from the group consisting of 2'-modified phosphodiester nucleotides, 2'-modified P-alkyloxyphosphotriester nucleotides; and wherein said 11 to 59 5' → 3'-linked nucleotides are divided by an RNase H-activating region which contiguously hybridizes to the RNA and comprises between three and ten contiguous phosphorothioate-linked deoxyribonucleotides, and wherein the 3' terminus of said oligonucleotide is drawn from the group consisting of: an inverted deoxyribonucleotide, a contiguous stretch of one to three phosphorothioate deoxyribonucleotides, phosphorothioate 2'-modified ribonucleotides, a biotin group, and a P-alkyloxyphosphodiester-linked nucleotide, and wherein the 5' terminus of said oligonucleotide is drawn from the group consisting of: an inverted deoxyribonucleotide, a contiguous stretch of one to three phosphorothioate deoxyribonucleotides, phosphorothioate 2'-modified ribonucleotides, a biotin group, and a P-alkyloxyphosphodiester-linked nucleotide.

19. (Once Amended) A chimeric antisense oligonucleotide comprising:

- a) an RNase H activation region which contiguously hybridizes to a specific RNA and which has between 5 and 10 contiguous deoxyphosphorothioate nucleotides;
- b) between 4 to 59 contiguous 5' → 3'-linked 2'-methoxyribonucleotides which contiguously hybridize to the specific RNA; and
- c) an exonuclease blocking group present at the 3' end, the 5' end, or both the 3' and 5' ends of the oligonucleotide drawn from the group consisting of: a non-5' → 3' phosphodiester-linked nucleotide, from one to three contiguous 5' → 3'-linked modified nucleotides, and a non-nucleotide chemical blocking group.